



Filariasis

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Patrick Manson

- Born Scotland, worked in China for 23 yrs
- Pioneer in tropical medicine
- Posted to Formosa (Taiwan) as MO for the Chinese Imperial Maritime Customs
- Kept diary; described elephantiasis, leprosy and "heart disease" (was beriberi)
- 1871 - settled at Amoy [Xiamen], port on the Chinese mainland
 - saw many cases of elephantiasis, developed surgical method for removing extra tissue.
- records show
 - he removed 1 ton of tissue/3 yrs
- Hypothesized and then proved via experiment with Hin-Lo that filariae are transmitted via mosquitoes

Filarial Worms

- Lymphatic filariasis
 - *Wuchereria bancrofti*, *Brugia malayi*, and *Brugia timori*
- Subcutaneous filariasis
 - *Loa loa*, *Mansonella streptocerca*, *Onchocerca volvulus*, and *Dracunculus medinensis*.
- Serous Cavity filariasis
 - *Mansonella perstans* and *Mansonella ozzardi*
- Other filaria
 - *Dirofilaria immitis*

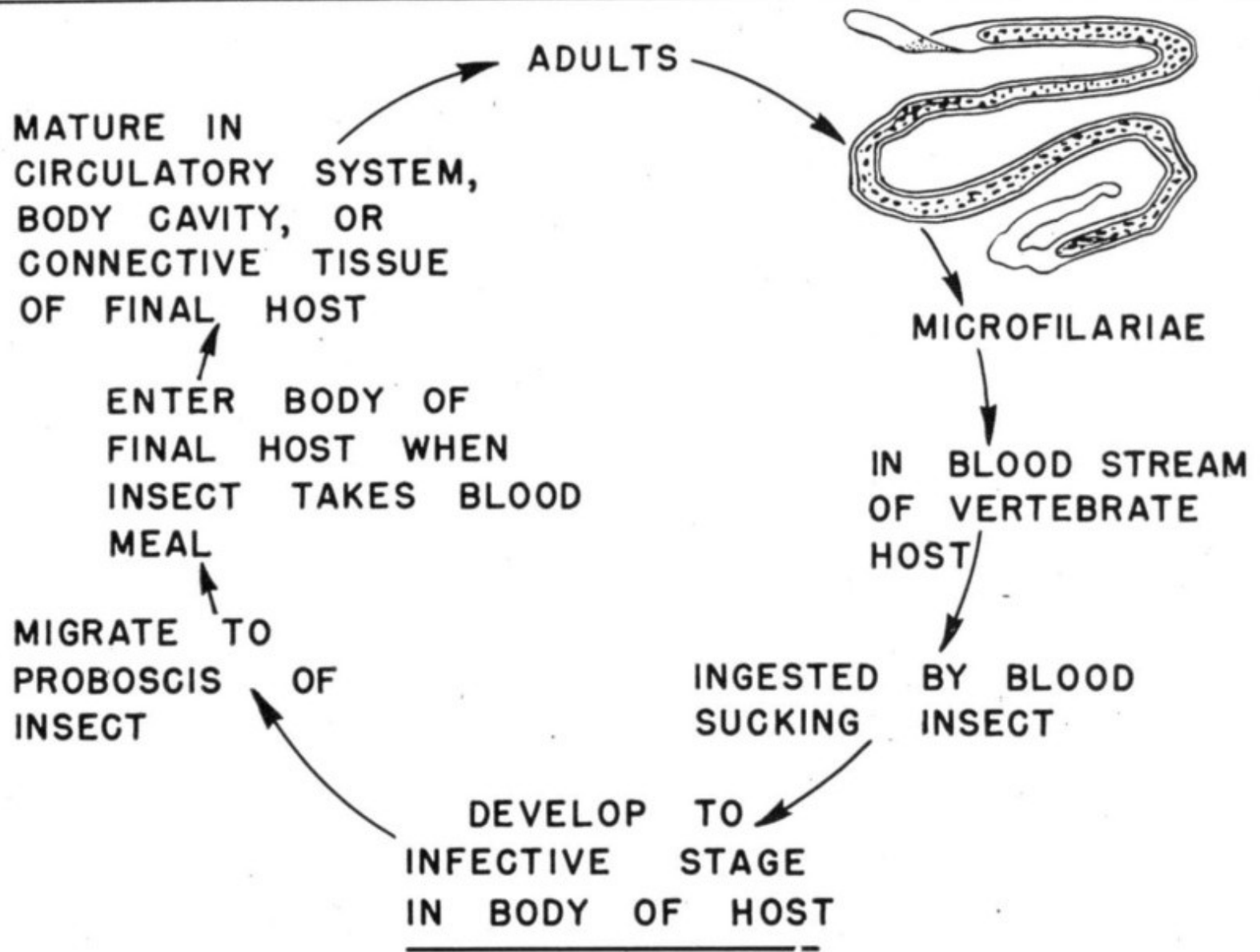
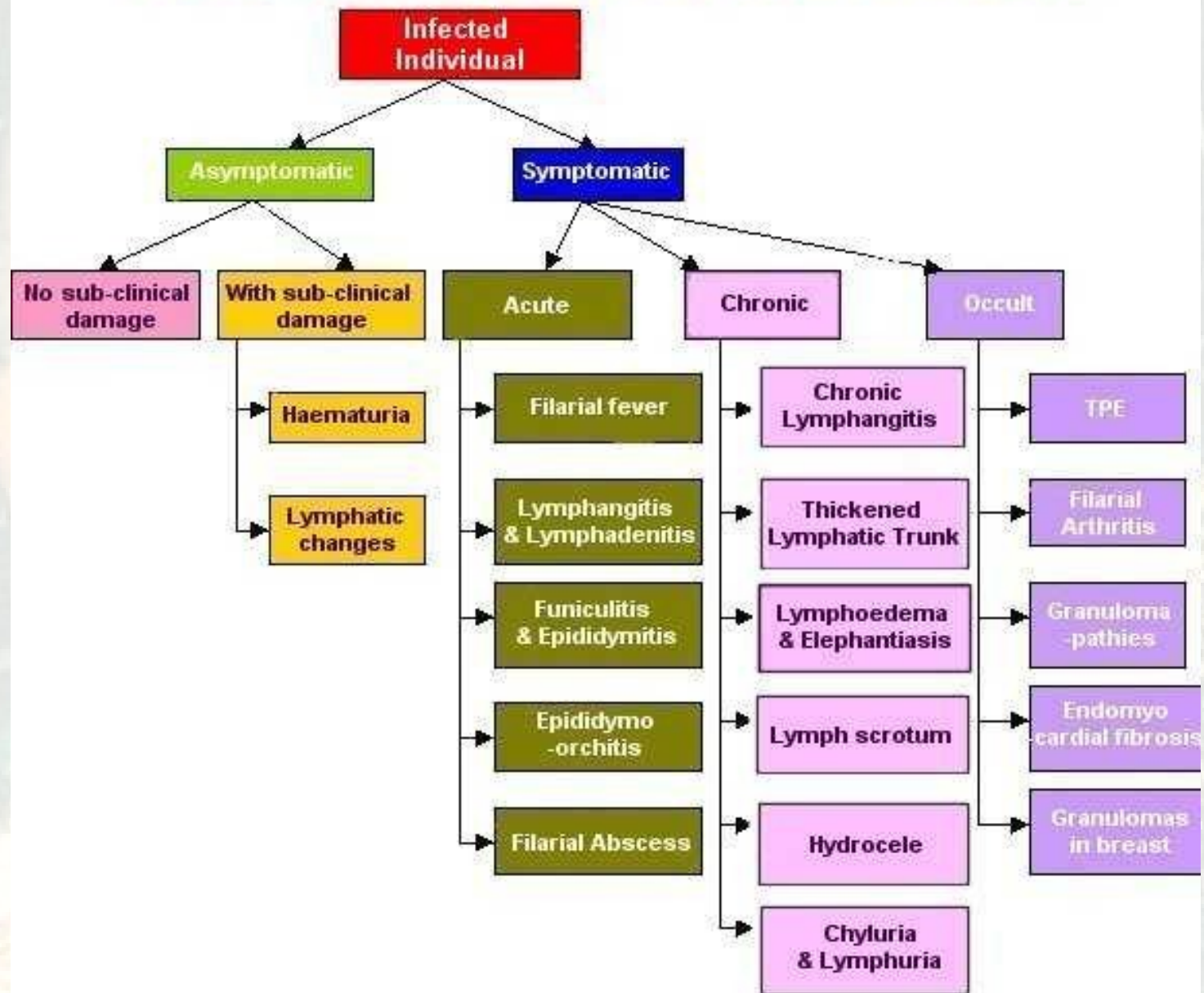
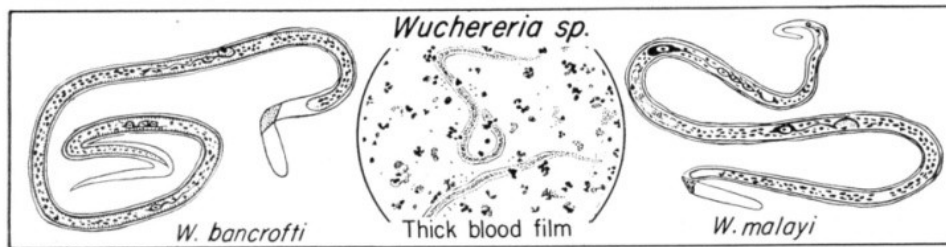


Fig. 179.—Nematode cycle—filarial worm type.

FILARIASIS DISEASE SPECTRUM CHART





FILARIASIS

HUMAN DISEASE —

Inflammatory Phase:

Lymphangitis and lymphadenitis
Orchitis, epididymitis, funiculitis

Filarial abscess, elephantoid fever

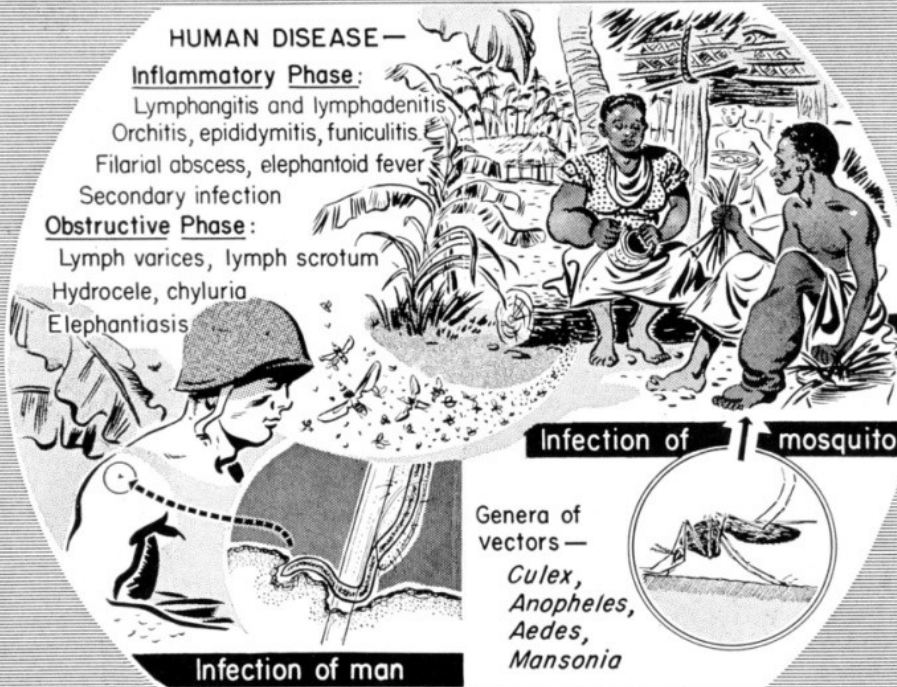
Secondary infection

Obstructive Phase:

Lymph varices, lymph scrotum

Hydrocele, chyluria

Elephantiasis



EPIDEMIOLOGY

1. Reservoir: man
2. Vectors: mosquitoes—several genera, many species
3. Mosquito ingests microfilariae
4. Development in mosquito thorax
5. Infected mosquito bites man
6. Infective larvae penetrate human skin
7. Mature parasites in lymphatic system
8. Microfilariae in peripheral blood

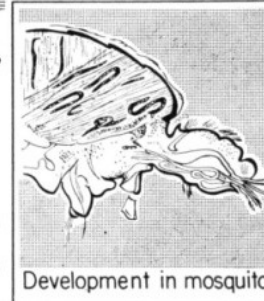
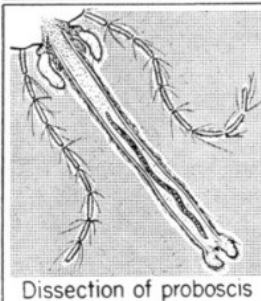
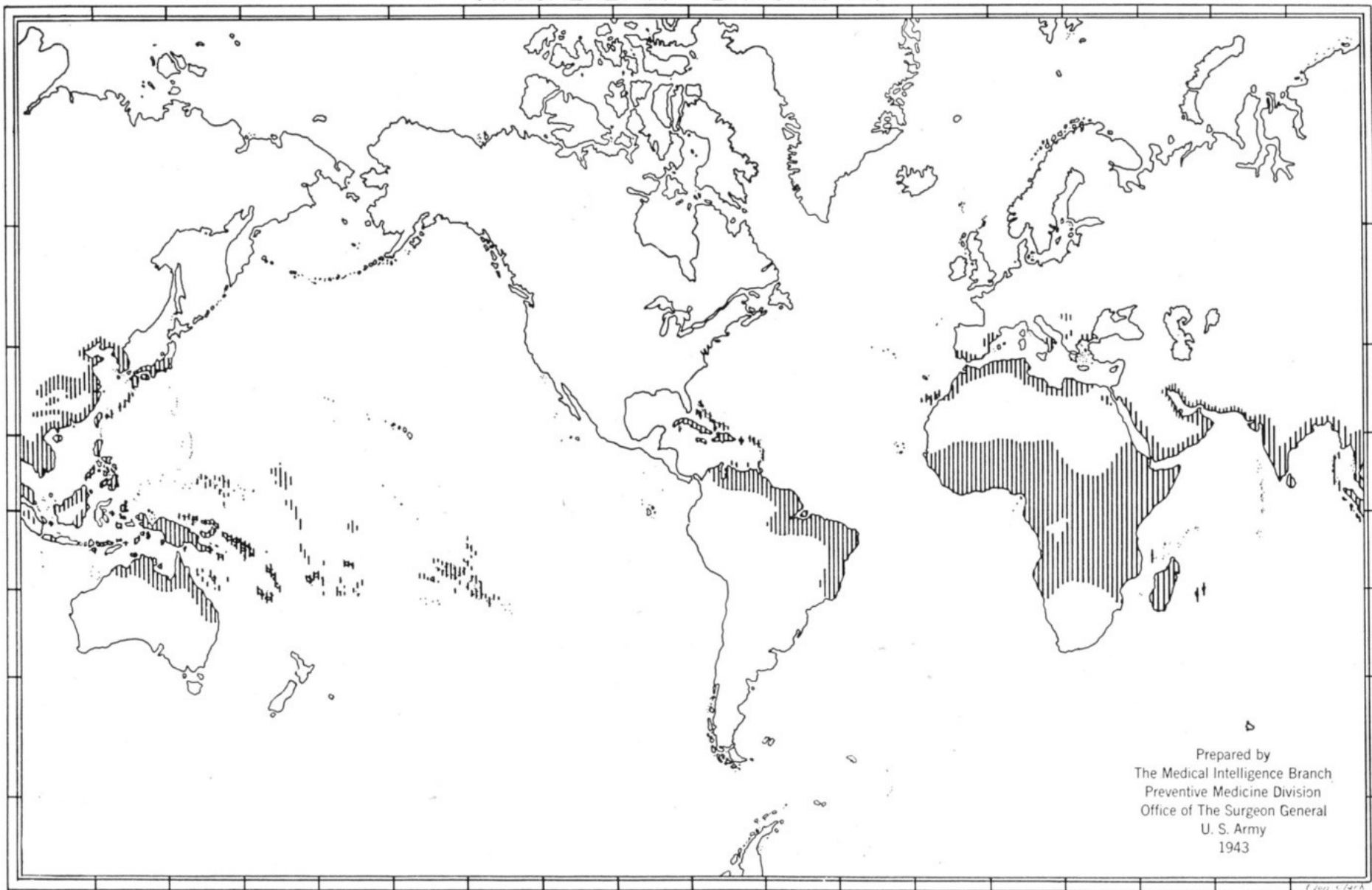


Fig. 182.—Epidemiology of filariasis.

FILARIASIS

(WUCHERERIA BANCROFTI)



Prepared by
The Medical Intelligence Branch
Preventive Medicine Division
Office of The Surgeon General
U. S. Army
1943

Fig. 180.—Geographical distribution of filariasis due to *Wuchereria bancrofti*.

Lymphatic Filariasis Endemic Countries and Territories



Endemic Countries



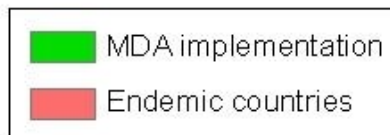
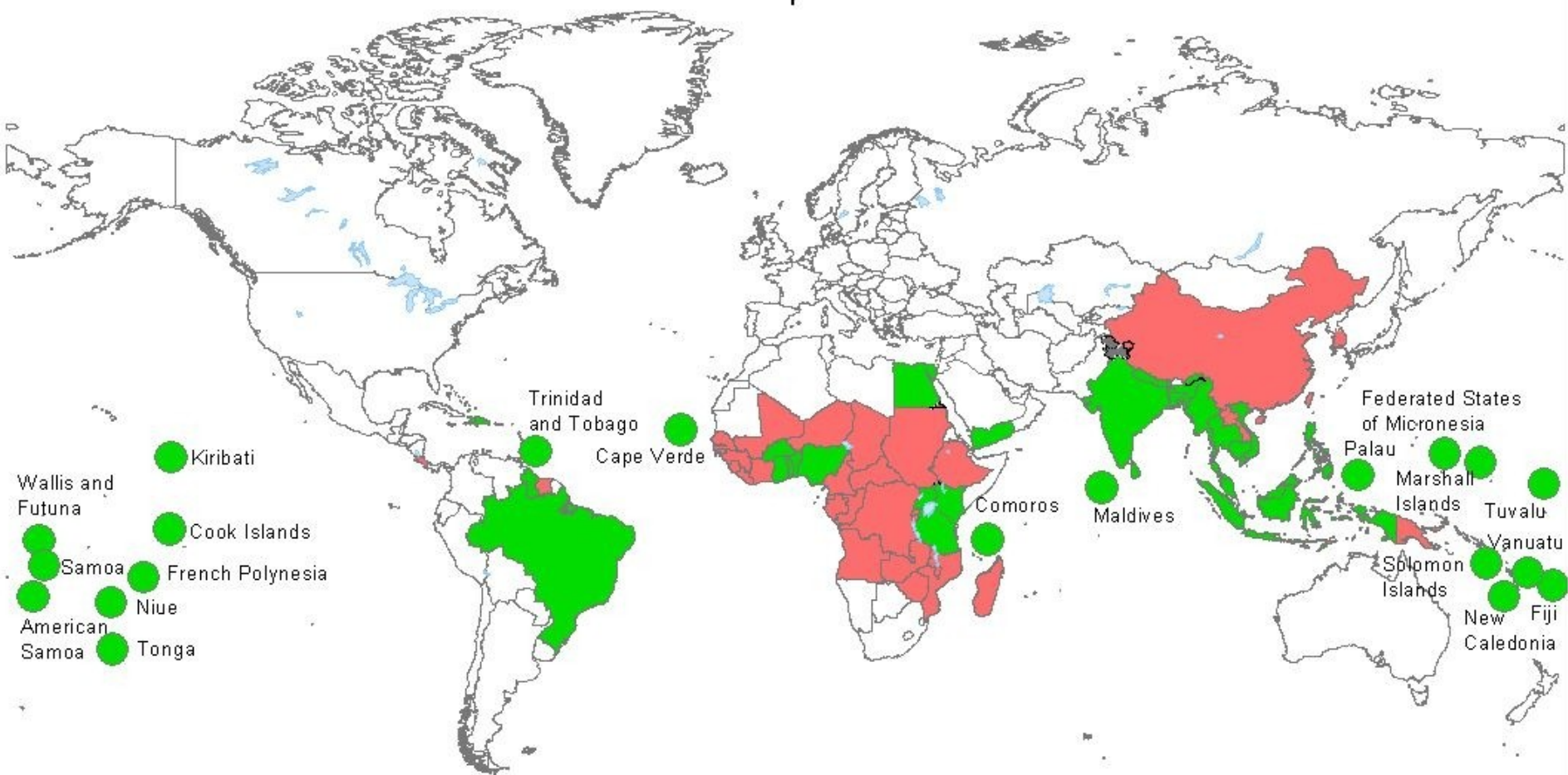
The presentation of material on the maps contained herein does not imply the expression of any opinion whatsoever on the part of the World Health Organization concerning the legal status of any country, territory, city or area or of its authorities, or concerning the delimitation of its frontiers or boundaries.



Data Source: Lymphatic Filariasis
Elimination Programme
Map Production:
Public Health Mapping
Communicable Diseases (CDI)
World Health Organization

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Lymphatic filariasis endemic countries currently under annual Mass Drug Administration (MDA)* As of April 2005



* China implemented MDA up to the 1990s



The boundaries and names shown and the designations used on this map do not imply the expression of any opinion whatsoever on the part of the World Health Organization concerning the legal status of any country, territory, city or area or of its authorities, or concerning the delimitation of its frontiers or boundaries. Dotted lines on maps represent approximate border lines for which there may not yet be full agreement.

Data Source: Lymphatic Filariasis Elimination Programme
Map Production:
Public Health Mapping & GIS
Communicable Diseases (CDS)
World Health Organization
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LF: a very morbid disease

Table 3. Infectious and parasitic diseases burden, worldwide and by region, 2001

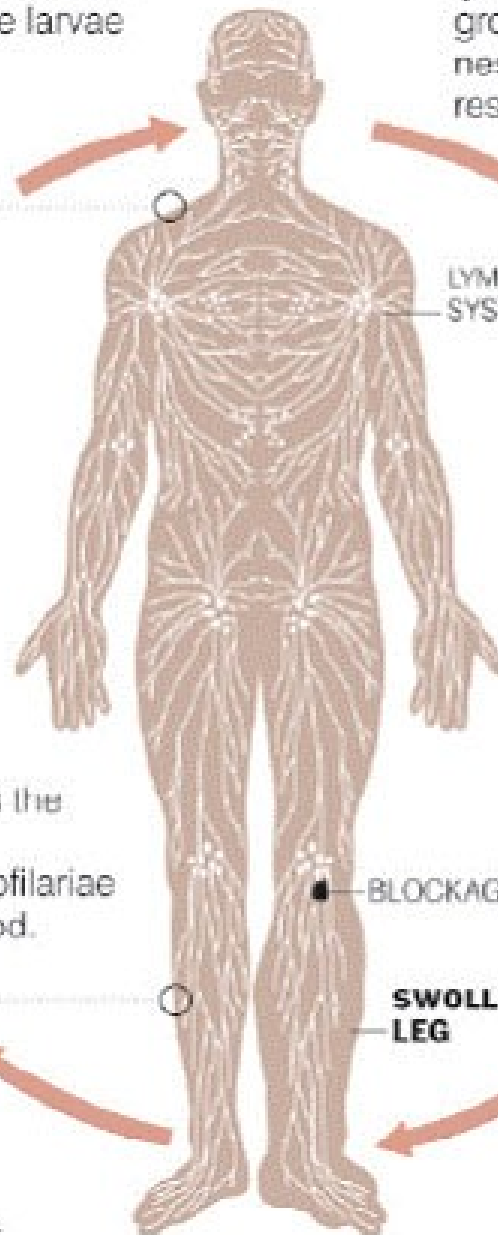
Disease	Disease burden worldwide, DALYs in thousands (%) ^a	Disease burden by region, % ^b					
		Africa	Southeast Asia	East Mediterranean	Western Pacific	The Americas	Europe
HIV/AIDS	88,429 (6.0)	65.0	15.4	1.9	2.2	3.1	1.0
Diarrheal disease	65,451 (4.3)	32.9	34.2	16.5	6.3	4.3	1.3
Malaria	42,280 (2.9)	85.2	8.7	4.8	1.0	0.3	0.1
Tuberculosis	36,040 (2.5)	24.8	44.3	8.3	15.3	2.6	4.7
Measles	26,495 (1.8)	57.1	26.1	11.5	4.4	0.0	0.9
Sexually transmitted disease ^c	12,404 (0.8)	41.4	34.8	10.7	5.1	5.1	2.9
Lymphatic filariasis	5,644 (0.4)	34.2	49.6	8.7	7.2	0.2	0.03
Trachoma	3,997 (0.3)	38.2	6.2	15.1	40.6	0.0	0.0
Leishmaniasis	2,357 (0.2)	17.0	67.3	11.8	1.1	2.5	0.3
Hookworm disease ^d	1,825 (0.1)	23.3	45.7	9.0	13.6	8.2	0.0
Schistosomiasis	1,760 (0.1)	80.6	0.2	11.5	2.9	10.4	0.0
Trichuriasis ^d	1,649 (0.1)	7.5	26.0	2.2	46.6	17.7	0.0
African trypanosomiasis	1,598 (0.1)	97.4	0.0	2.5	0.0	0.0	0.0
Ascariasis ^d	1,181 (0.1)	10.2	22.8	5.2	46.4	14.6	0.7
Onchocerciasis	987 (0.1)	95.0	0.0	4.7	0.0	0.3	0.0
Japanese encephalitis	767 (0.1)	0.0	45.2	10.6	44.3	0.0	0.0
Dengue	653 (0.0)	0.9	55.1	13.0	17.2	13.8	0.0
Chagas disease	649 (0.0)	0.0	0.0	0.0	0.0	99.8	0.0
Leprosy	177 (0.0)	9.0	67.2	9.0	4.0	10.2	0.0
All infectious and parasitic diseases	359,377 (24.5)	52.6	26.2	9.7	6.4	3.5	

The Life Cycle of Lymphatic Filariasis

1 An infected mosquito deposits larvae on the skin while biting and the larvae enter the wound.



2 The larvae migrate to the lymphatic system, where they grow, mate and form nests. The nests cause blockages, resulting in swelling and fever.



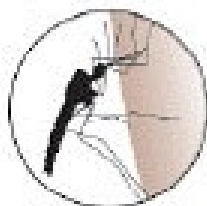
ADULT
WORMS



5 Microfilariae develop into larvae over a period of a week.



4 A mosquito bites the infected person, ingesting the microfilariae along with the blood.



3 Female worms produce microscopic worms called microfilariae, below, that swarm in the blood at night, when mosquitoes bite.

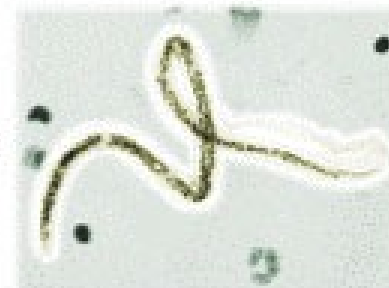


Photo from C.D.C.

1. *Agave* *deserti* *Agave* *deserti* *Agave* *deserti*

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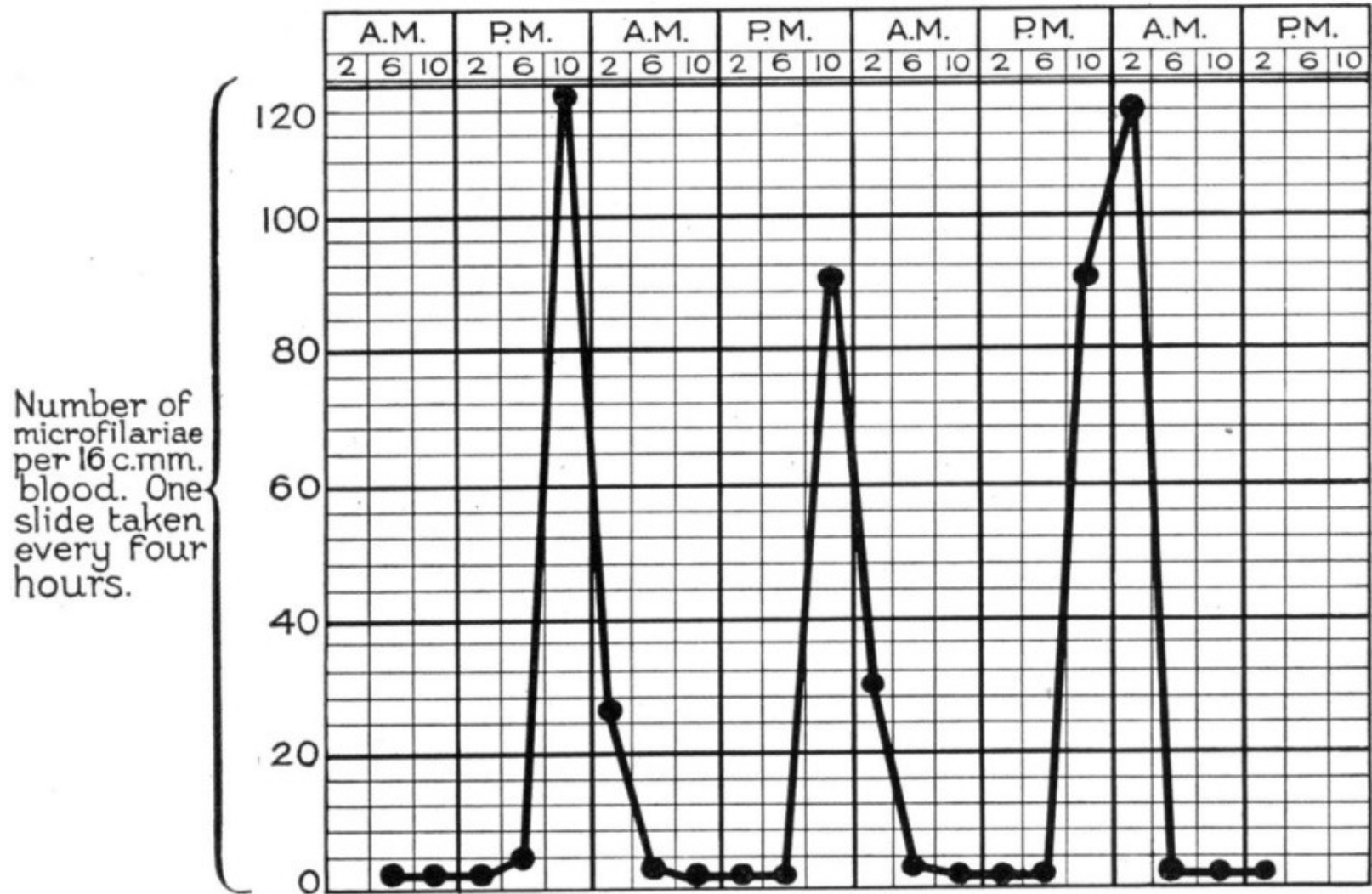
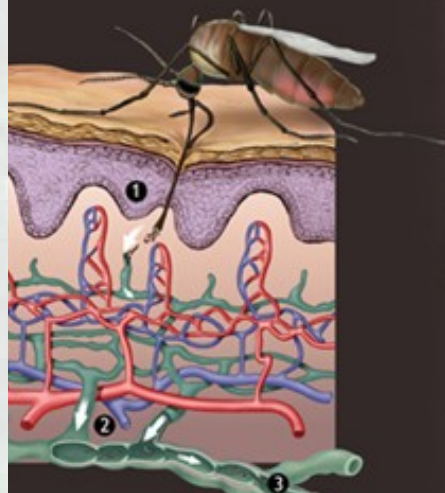


Fig. 178.—Periodicity of *Wuchereria bancrofti* in peripheral blood. (After Manson-Bahr in Strong: Stitt's Diagnosis, Prevention and Treatment of Tropical Diseases. The Blakiston Company.)



A. INITIAL ACUTE RESPONSE:

Parasite-specific local inflammatory reaction
(cell-mediated and humoral components).
Inflammatory infiltrate surrounds and attacks worm

B. GRANULOMATOUS REACTION:

Release of endosymbiotic intracellular bacteria
(*Wolbachia* sp.) as worm is digested.
TNF- α (tumour necrosis factor) is induced followed
by a granulomatous inflammatory response.

1. Infected mosquito releases
B. malayi microfilariae
(larvae)

2. Microfilariae migrate to
lymph capillary and into
lymphatic vessels

3. Maturation of larvae into
adult worms (3-12 months
in circulation)

4. Vessel dilation

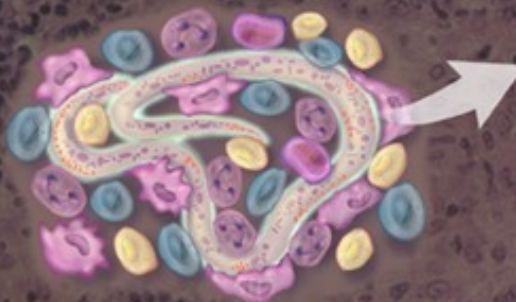
5. Intramural polyposis

6. Hypertrophy of vessel walls

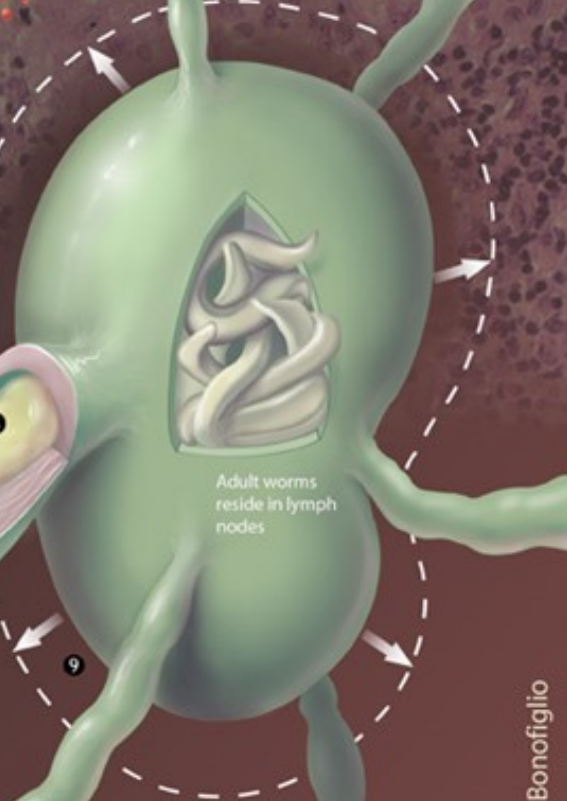
7. Fibrosis in vessel walls
due to granulomatous
inflammatory response

8. Back up of lymph in vessel

9. Lymph node enlargement



©Marisa Bonofiglio



Adult worms
reside in lymph
nodes

LYMPHATIC FILARIASIS : inflammatory response to *Wolbachia* bacteria in filarial worms

LF: clinical manifestations



elephantiasis

LF: clinical manifestations



19yo Haitian man
May 2009

courtesy Dr. Todd Gleeson, USS Comf

LF: clinical manifestations



Courtesy Dr. Todd Gleeson, USS Comf

LF: clinical manifestations



Courtesy Dr. Todd Gleeson, USS Comf

Treatment

- Annual treatment of all individuals at risk (individuals living in endemic areas) with recommended anti-filarial drugs combination
 - diethyl-carbamazine citrate (DEC) and albendazoleor
 - ivermectin and albendazoleor
 - regular use of DEC fortified salt can prevent occurrence of new infection and disease



ONCHOCERCIASIS, LOIASIS AND FILARIASIS MALAYI

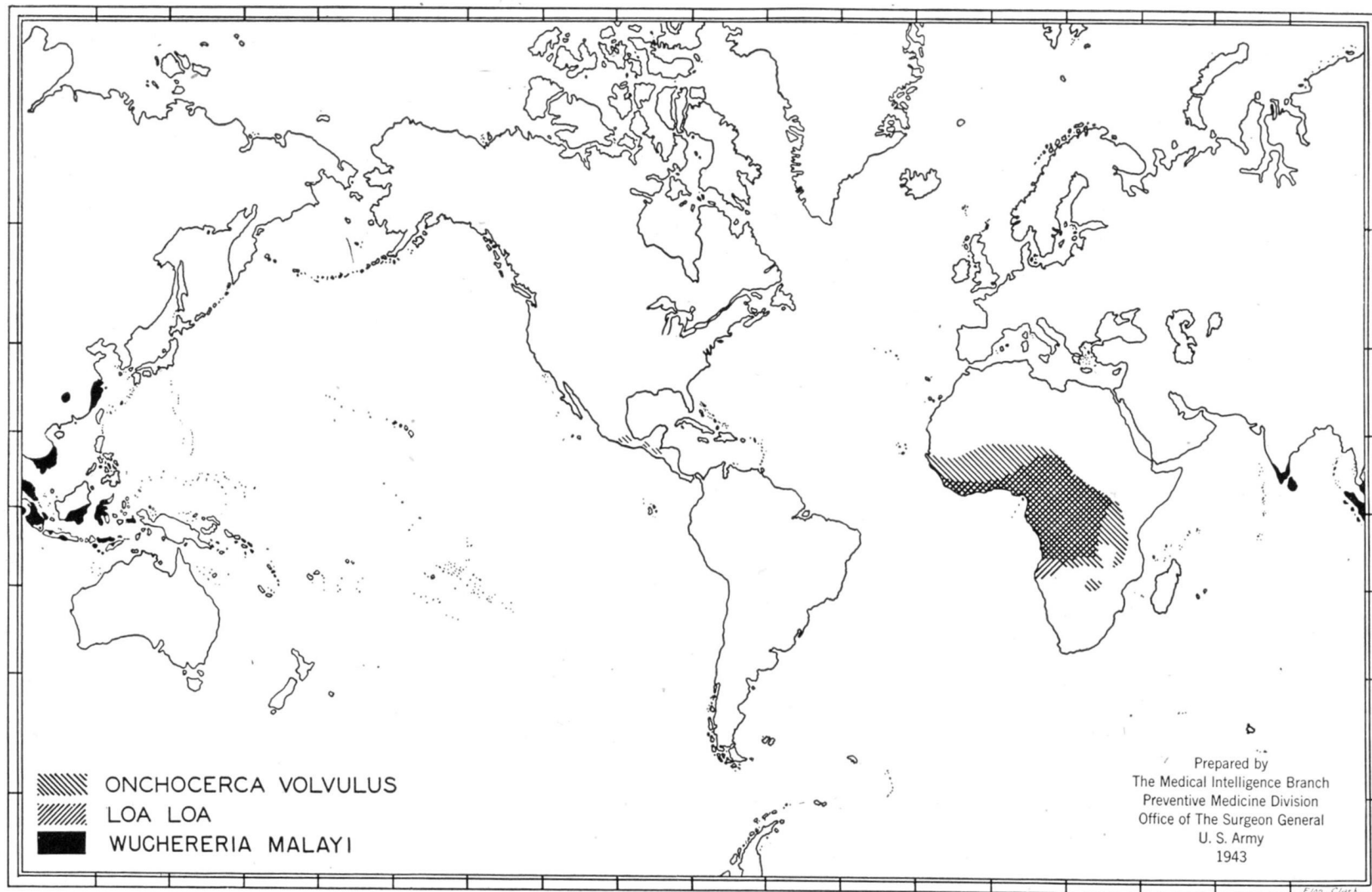


Fig. 193.—Geographical distribution of onchocerciasis, loiasis, and filariasis malayi.

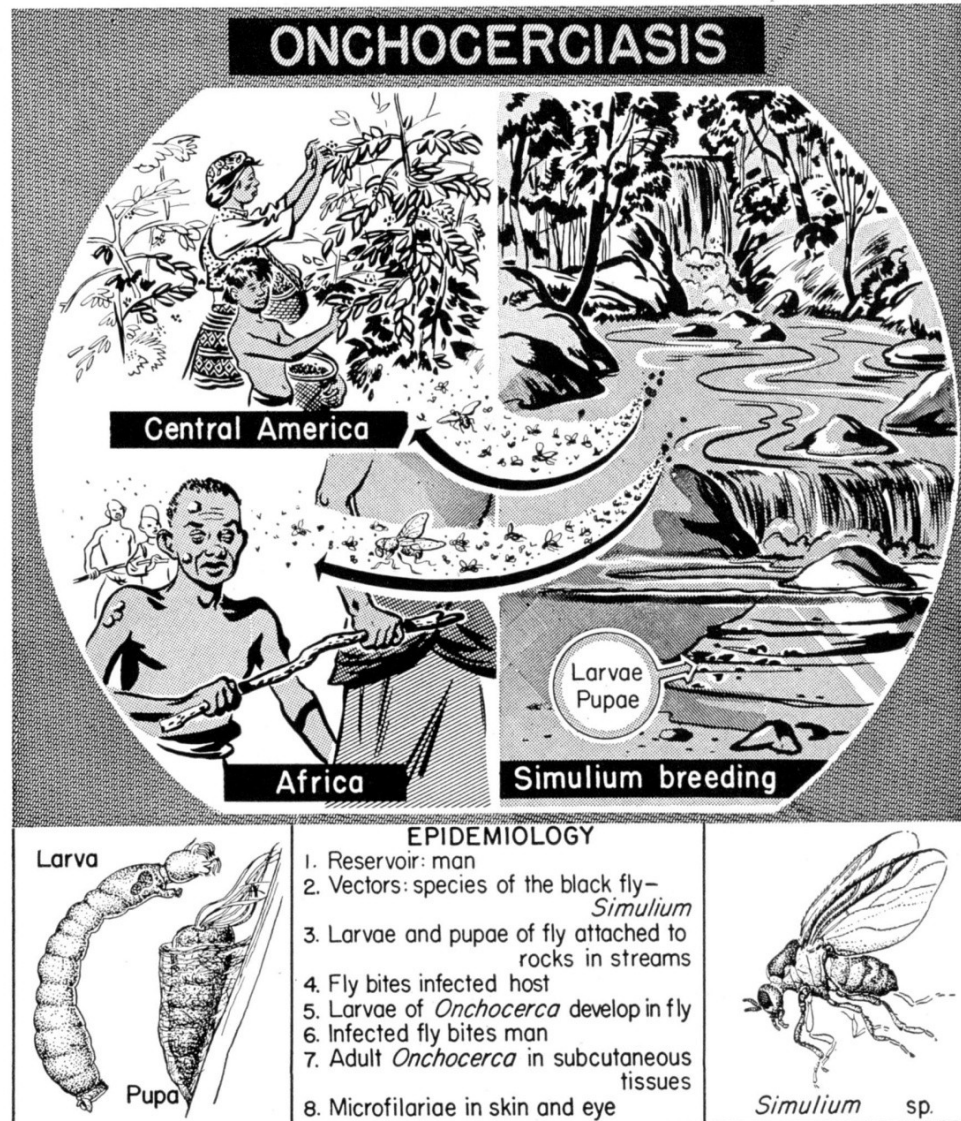


Fig. 194.—Epidemiology of onchocerciasis.

Onchocercal dermatitis



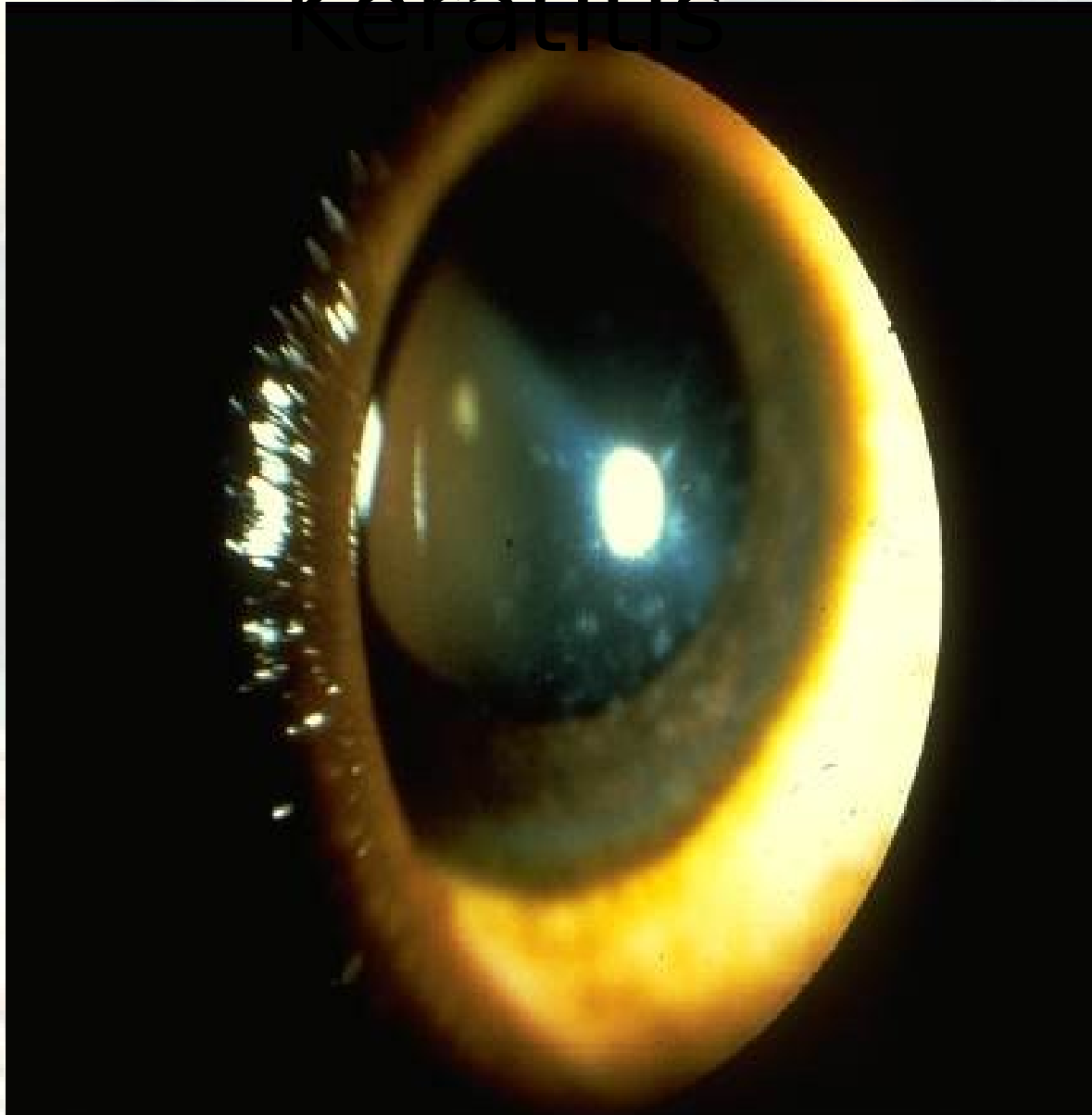
Onchocercal dermatitis



Onchocerciasis - Sowda



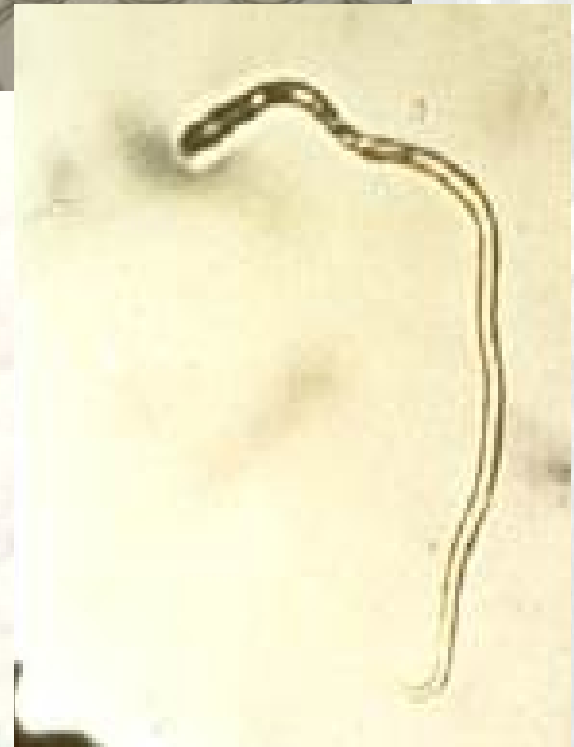
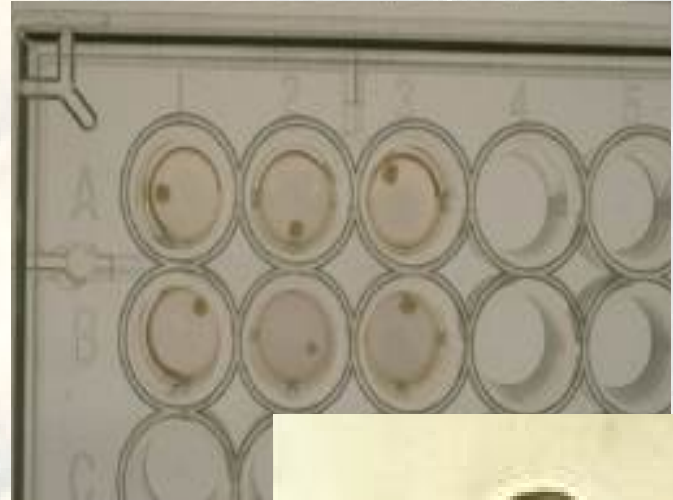
Onchocerciasis – Punctate Keratitis



Onchocerciasis - Sclerosing Keratitis



Onchocerciasis: skin snips



Treatment

- Ivermectin (150–200 µg/kg orally, once or twice per year) is the drug of choice for onchocerciasis.
- Repeated annual or semiannual doses may be required (drug kills the microfilariae but not the adult worms)
- Antibiotic trials with doxycycline (100 mg orally per day) directed against *Wolbachia*, an endosymbiont of *O. volvulus*, have demonstrated a decrease in onchocercal microfilaridemia with 6 weeks of therapy
- Some experts recommend treating patients with 1 dose of ivermectin followed by 6 weeks of doxycycline
- Diethylcarbamazine (DEC) is contraindicated in onchocerciasis!!! (associated with severe and fatal posttreatment reactions)

History of Presenting Illness

- 33 y/o Nigerian female
- Lived in U.S. for last 2.5 years
- 2 weeks post-op for resection of left foot pyogenic granuloma
- Re-admitted for surgical site infection

History of Presenting Illness

- Plain films of left foot demonstrated possible subcutaneous gas
- Patient was s/p debridement on hospital day #1 when ID was consulted for antibiotic recommendations
- Claimed to have a fever, denied chills
- Wound discharge noted, blood cultures taken

History

- PMHx: none
- PSHx: C-Section x 2
- Meds: Zosyn (Pip/Tazo) 3.375g IV q6h
- All: NKDA
- SHx: Tob: none, EtOH none, Drugs none
- FHx: Non-Contributory
- Travel: none recent, last in Nigeria 2.5 yrs ago;

Physical Examination

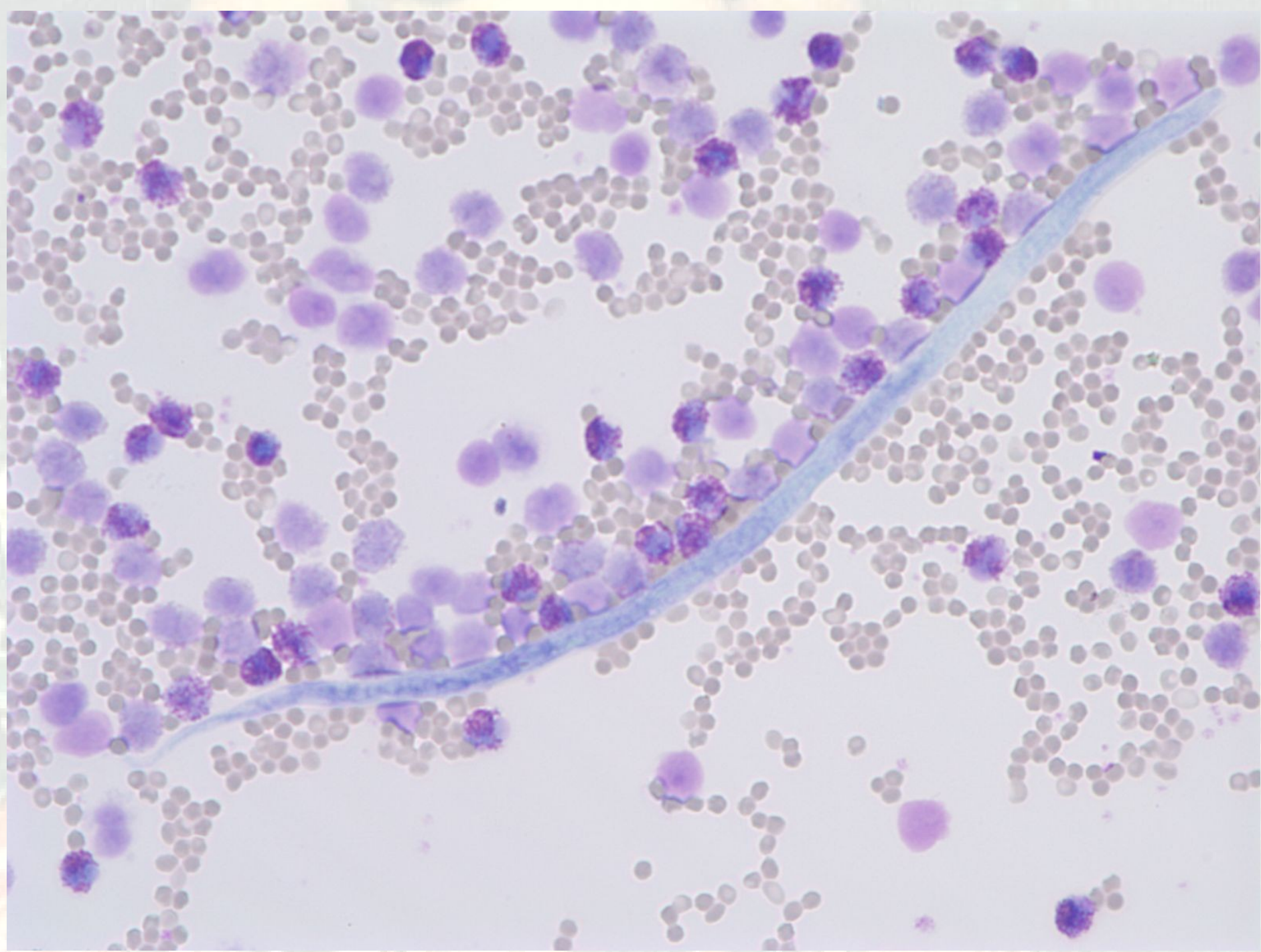
- Vitals: T=97.8°F; BP=130/90; HR=88; RR=16
- HEENT: Normal
- Lung: Clear
- Cardiac: RRR nl s1/s2; I/VI SEM LSB
- Abd: benign
- Ext: RLE WNL; LLE wrapped and elevated
- LN: + shotty inguinal LN, + palpable SQ nodule medial thigh, mildly TTP

Laboratory

- Wound Cx: many WBC, Mod GPC pairs, few small GNR
- WBC=8.1 HCT=37.0 PLT=232
- Poly=32 Lymph=28 Mono=7
Eos=32 Baso=1
- Na=143 K=4.1 Cl=99 HCO3=27
- BUN=13 Cr=0.8 Ca=9.5 Glu=90

Laboratory (cont.)

- Blood cultures taken at presentation turned positive
- Gram stain performed did not reveal bacteria
- Organism was found on differential slide
- Simultaneously, wet mount made



	TESTS	RESULT	FLAG	UNITS	REFERENCE INTERVAL	LAB				
	CBC WITH DIFFERENTIAL/PLATELET									
	White Blood Cell (WBC) Count	8.1		X 10 ⁻³ /uL	4.0 - 10.5	A				
	Red Blood Cell (RBC) Count	4.78		X 10 ⁻⁶ /uL	3.80 - 5.10	A				
	Hemoglobin	12.1		g/dL	11.5 - 15.0	A				
	Hematocrit	37.0		%	34.0 - 44.0	A				
	MCV	77	L	fL	80 - 98	A				
	MCH	25.3	L	pg	27.0 - 34.0	A				
	MCHC	32.7		g/dL	32.0 - 36.0	A				
	RDW	18.0	H	%	11.7 - 15.0	A				
	Platelets	232		X 10 ⁻³ /uL	140 - 415	A				
	Polys	32	L	%	40 - 74	A				
	Lymphs	28		%	14 - 46	A				
	Monocytes	7		%	4 - 13	A				
	Eos	32	H	%	0 - 7	A				
	Basos	1		%	0 - 3	A				
	Polys (Absolute)	2.6		X 10 ⁻³ /uL	1.8 - 7.8	A				
	Lymphs (Absolute)	2.3		X 10 ⁻³ /uL	0.7 - 4.5	A				
	Monocytes(Absolute)	0.6		X 10 ⁻³ /uL	0.1 - 1.0	A				
	Eos (Absolute Value)	2.6	H	X 10 ⁻³ /uL	0.0 - 0.4	A				
	Baso(Absolute)	0.1		X 10 ⁻³ /uL	0.0 - 0.2	A				
	Hematology Comments:	Note:				A				
	Differential reviewed and confirmed.									
	MICRO-FILARIA SEEN ON PERIPHERAL SMEAR. PATHOLOGIST TO REVIEW.									
	MANSONELLA PIRSTANS / STREPTOCERCA					A				
	BASIC METABOLIC PANEL (8)									
	Glucose, Serum	90		mg/dL	65 - 109	A				
	BUN	11		mg/dL	5 - 26	A				
	Creatinine, Serum	0.8		mg/dL	0.5 - 1.5	A				
	BUN/Creatinine Ratio	13								
	Sodium, Serum	143		mmol/L	135 - 148	A				
	Potassium, Serum	4.1		mmol/L	3.5 - 5.5	A				
	Chloride, Serum	99		mmol/L	96 - 109	A				
	Carbon Dioxide, Total	27		mmol/L	20 - 32	A				
	Calcium, Serum	9.5		mg/dL	8.5 - 10.6	A				

LAB: AV LABCORP HERNDON DIRECTOR: YASMEEN HAIDER MD
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REPORT

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Verification

- Patient info, slides, and video brought to third party for examination and comment
- Attempts at restraining of slides made
- Features on organisms noted that brought original diagnosis into question



Keys to Diagnosis

- Location of microfilariae
- Periodicity
- Morphology
 - Sheath
 - Cephalic head
 - Excretory pore

Table 11. Common Human Filarial Parasites.*

CHARACTERISTICS	<i>WUCHERERIA BANCROFTI</i>	<i>BRUGIA MALAYI</i>	<i>LOA LOA</i>	<i>MANSONELLA PERSTANS</i>	<i>MANSONELLA OZZARDI</i>	<i>MANSONELLA STREPTOCERCA</i>	<i>ONCHOCERCA VOLVULUS</i>
Geographic distribution	Cosmopolitan; tropics and subtropics	Asia, Indian sub-continent	West and Central Africa	Africa, South and Central America	South and Central America, Caribbean	West and Central Africa	Africa, Central and South America
Adult habitat	Lymphatic system	Lymphatic system	Subcutaneous tissues	Body cavities, mesenteries, perirenal and retroperitoneal tissues (?)	Subcutaneous tissues	Subcutaneous tissues	Subcutaneous tissues
Vector	Mosquitoes	Mosquitoes	<i>Chrysops</i> (deer fly)	<i>Culicoides</i> (midge)	<i>Culicoides</i> , <i>Simulium</i>	<i>Culicoides</i> (midge)	<i>Simulium</i> (black fly)
Location of microfilariae	Blood	Blood	Blood	Blood	Blood	Skin	Skin
Periodicity	Nocturnal†	Nocturnal‡	Diurnal	None	None	None	None
Morphology of microfilariae:							
Sheath	Present	Present	Present	Absent	Absent	Absent	Absent
Length (µm)							
Smears	244-296 (260)	177-230 (220)	231-250 (238)	190-200 (195)	163-203 (183)	—	—
2% Formalin	275-317 (298)	240-298 (270)	270-300 (281)	183-225 (203)	203-254 (224)	—	—
Skin snips	—	—	—	—	—	—	—
Width (µm)	7.5-10.0	5-6	5-7	4-5	3-5	180-240 (210)	304-315 (309)
Tail and tail nuclei	Tapered to point; no nuclei in end of tail	Tapered; terminal and subterminal nuclei	Tapered; nuclei irregularly spaced to end of tail	Tapered, bluntly rounded; nuclei to end of tail	Long, slender tail; no nuclei in end of tail	Tapered, bluntly rounded; nuclei to end of tail. Tail bent in hook shape	Tapered to point; no nuclei in end of tail

* Modified from Smith et al, 1976a. Used by permission.

† Subperiodic in Pacific islands.

‡ Subperiodic form as well.

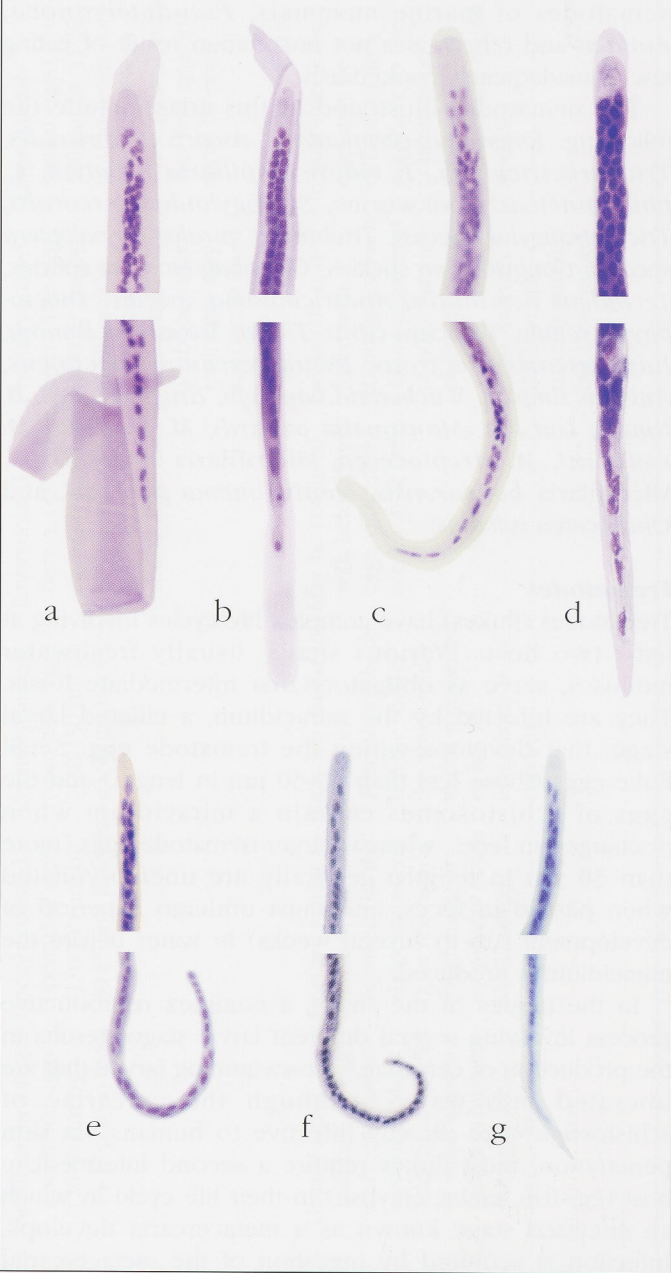


Figure 10. Anterior and posterior ends of microfilariae found in humans: *Wuchereria bancrofti* (a), *B. malayi* (b), *O. volvulus* (c), *Loa loa* (d), *Mansonella perstans* (e), *M. streptocerca* (f), and *M. ozzardi* (g). Modified from Smith et al, 1976a. Used by permission.

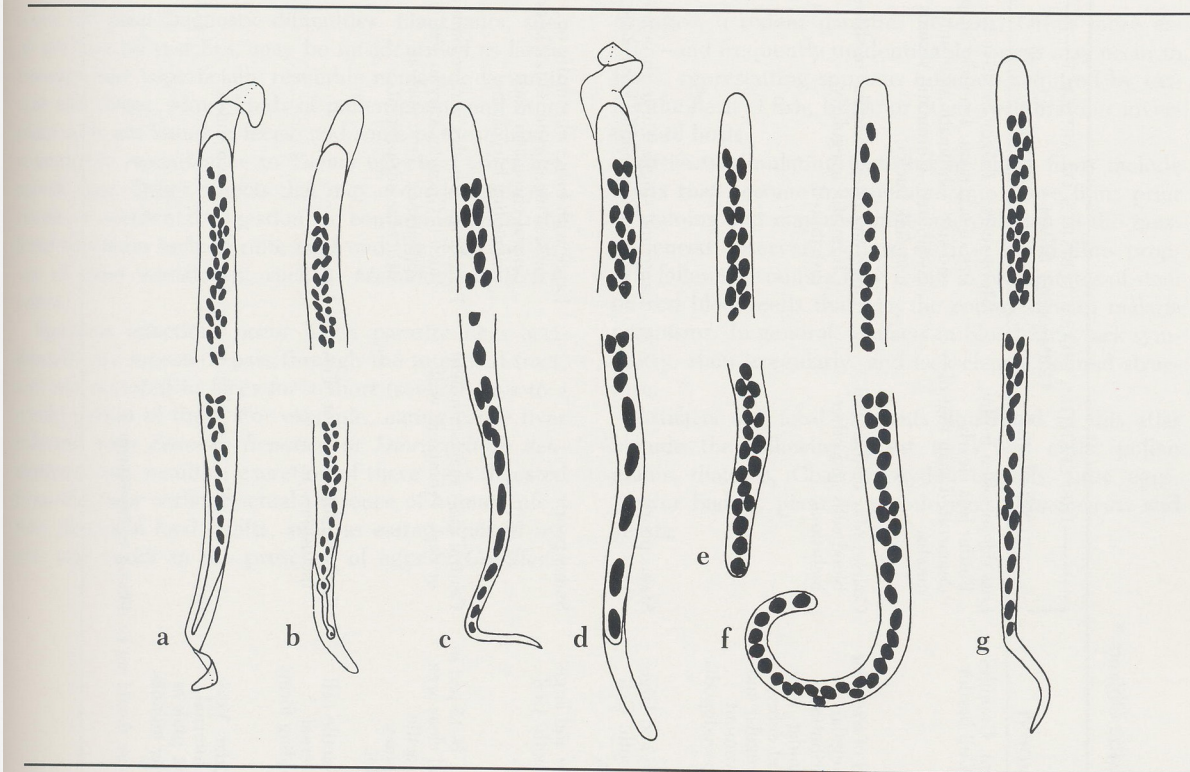
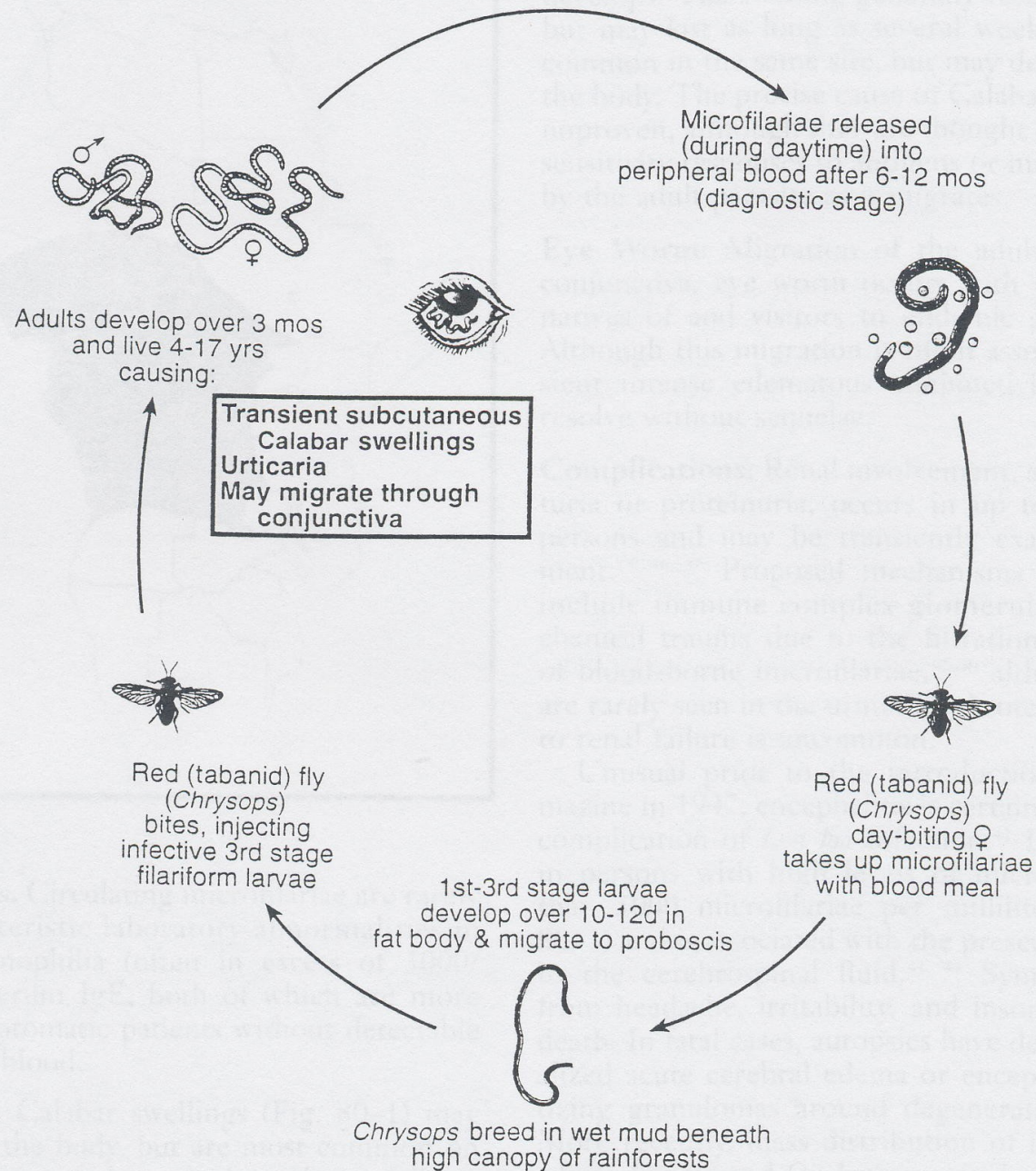


Figure 6. Anterior and posterior ends of microfilariae found in humans: *Wuchereria bancrofti* (a), *Brugia malayi* (b), *Onchocerca volvulus* (c), *Loa loa* (d), *Mansonella perstans* (e), *M. streptocerca* (f), and *M. ozzardi* (g). Modified from Smith et al, 1976a. Used by permission.

Loa loa



Loiasis - Clinical

- Calabar Swellings
- Eye Worm
- Pruritis
- Pain
- Fatigue, fever, arthritic pain
- Eosinophilia (up to 75%)
- Encephalitis – rare, associated with therapy

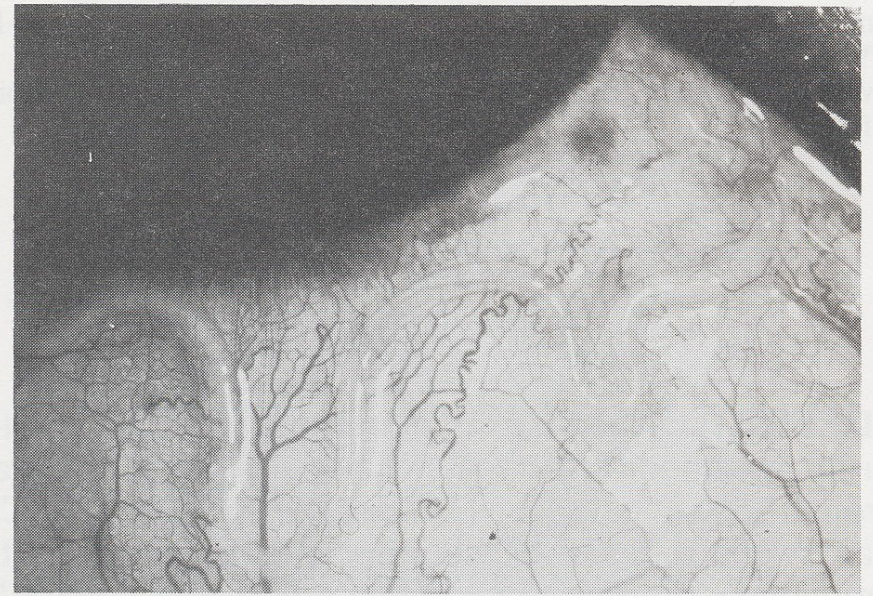


FIGURE 86-1. Adult *Loa* worm migrating beneath conjunctiva. (Courtesy of Dr. J. Anderson.)

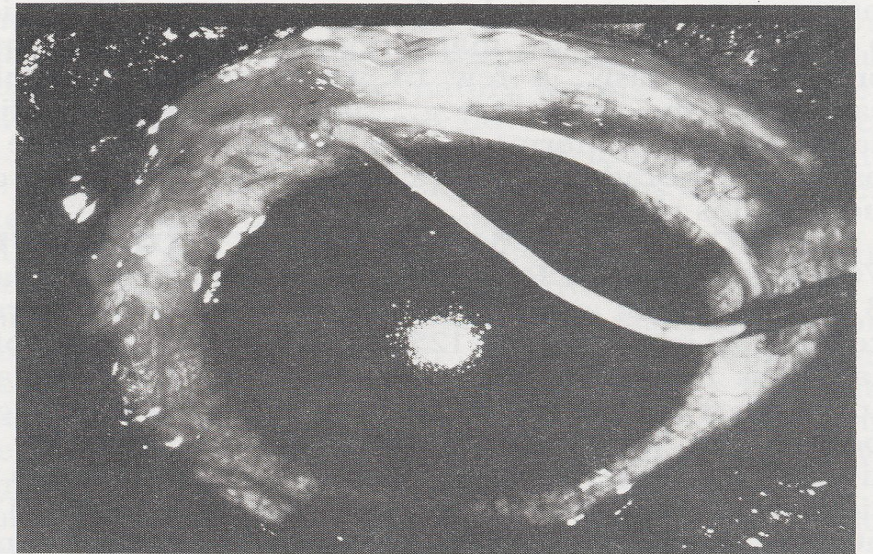
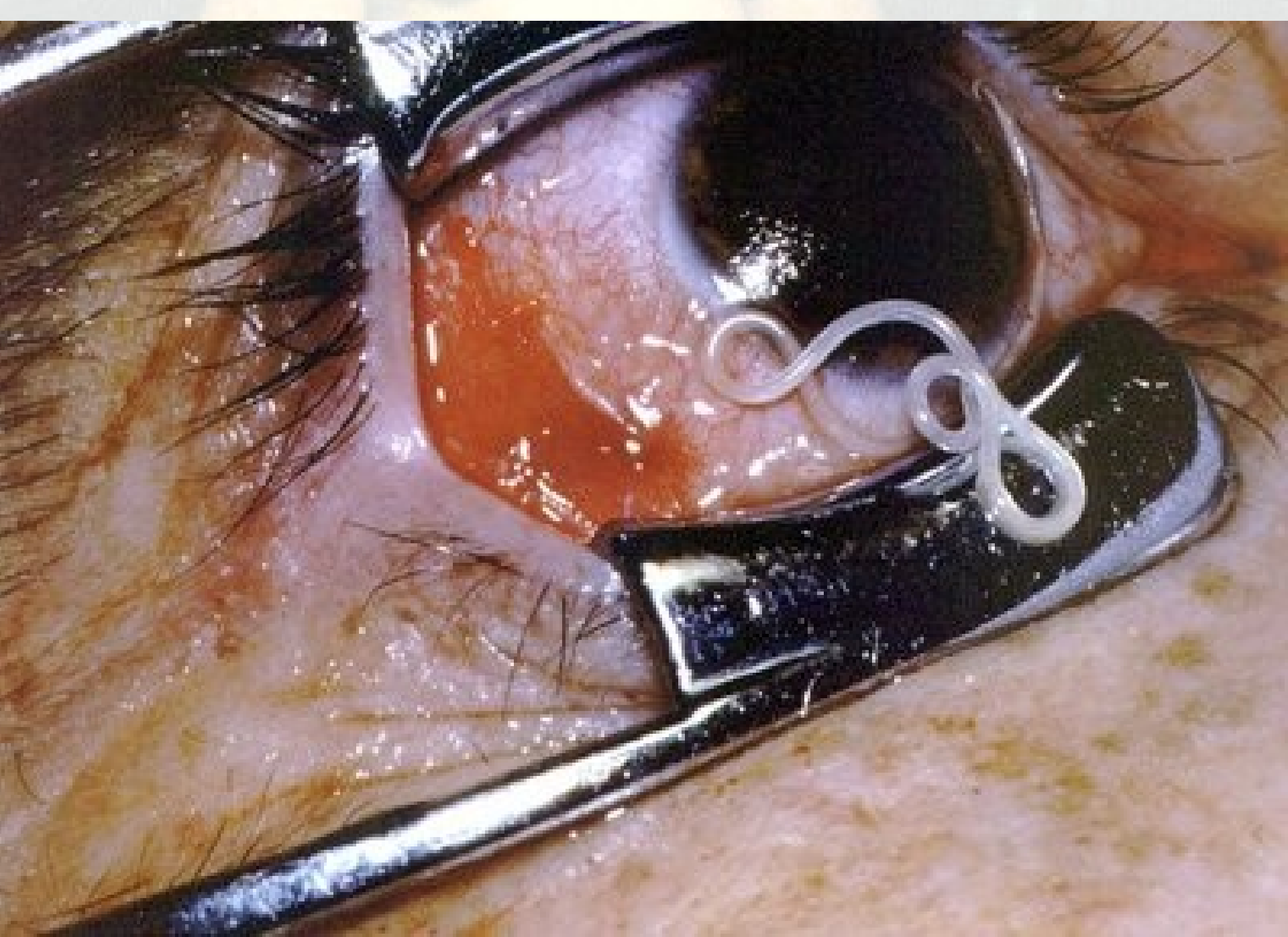


FIGURE 86-4. Surgical removal of *Loa* worm from eye. (Courtesy of the Armed Forces Institute of Pathology. Photograph Neg. No. 75-1789-4.)



FIGURE 86-2. Zairian woman with Calabar swelling around left eye. (Courtesy of the Armed Forces Institute of Pathology. Photograph Neg. No. 68-7638-15.)



Loiasis - Therapy

- Diethylcarbamazine (DEC) is Drug of Choice since 1951
 - 5 mg/kg in divided doses qd for 21 days
 - Kills microfilariae
 - Slower against adults
 - Given in escalating doses
 - May give with steroids
 - Consider plasapheresis if available
 - Adverse Drug Reactions: urticaria, fever, nausea, encephalitis

IT'S NOT OVER UNTIL THE LAST WORM IS GONE...

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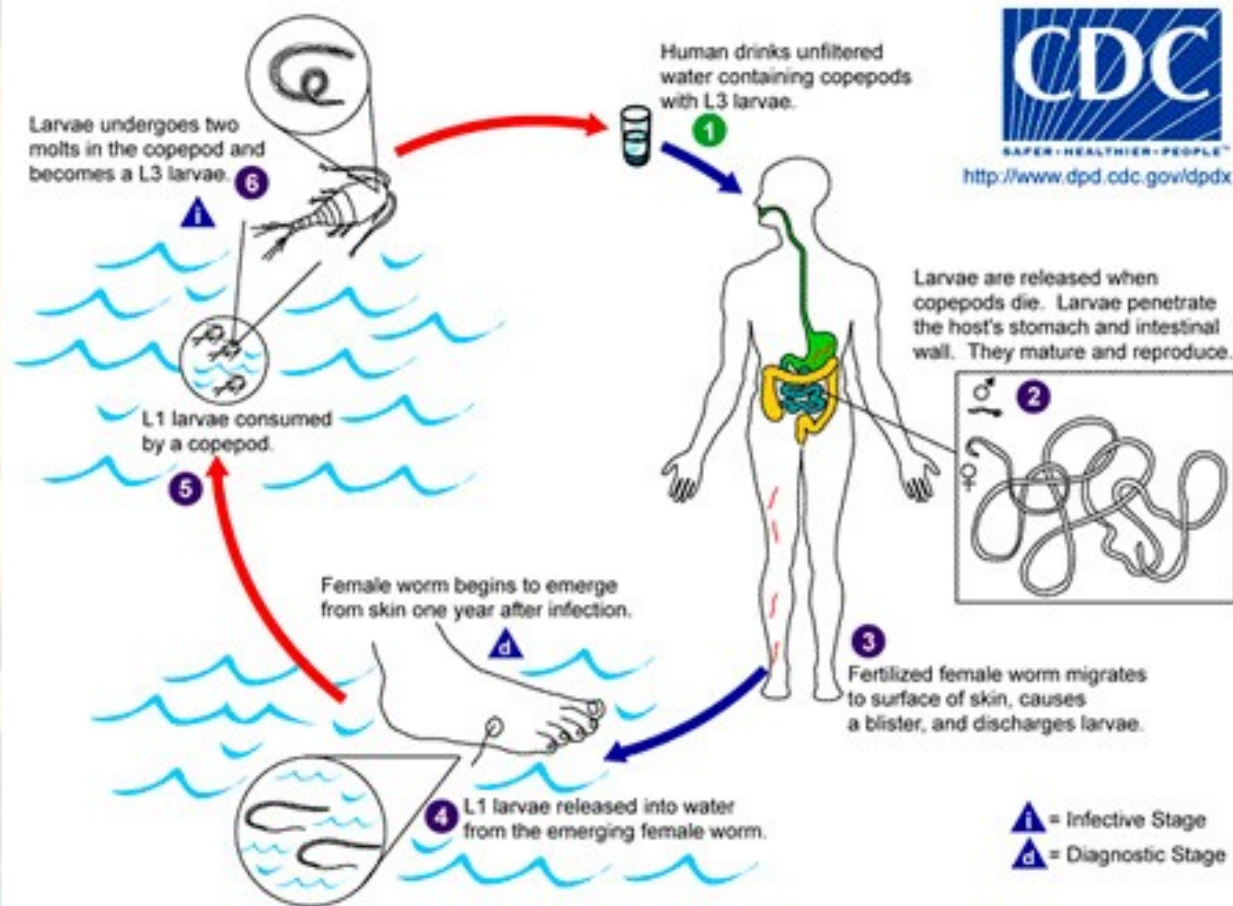
CELE



- “The fiery serpent” that afflicted the Israelites during their exodus
- Disease is more than 3,000 years old - discovered in calcified mummies
- Big enough scourge that it was recognized by Greek, Roman and Arab-Persian philosophers and physicians; indisputably a disease of antiquity
- May not be a human disease of the future
- Global eradication efforts spearheaded by the Carter Center in 1986--in partnership with WHO, CDC and UNICEF--have slashed the incidence
 - 1986, there were an estimated 3.5 million cases of Guinea worm in 20 countries in Africa and Asia
 - 2008, there were just 4,587 documented cases in 5 countries all within sub-Saharan Africa
- Soon to become the first parasitic disease to be eradicated--and second human disease to be eradicated, after smallpox.
- Furthermore, eradication would be achieved solely by behavioral measures, not by a vaccine or cure (as was done with smallpox)



Life Cycle:

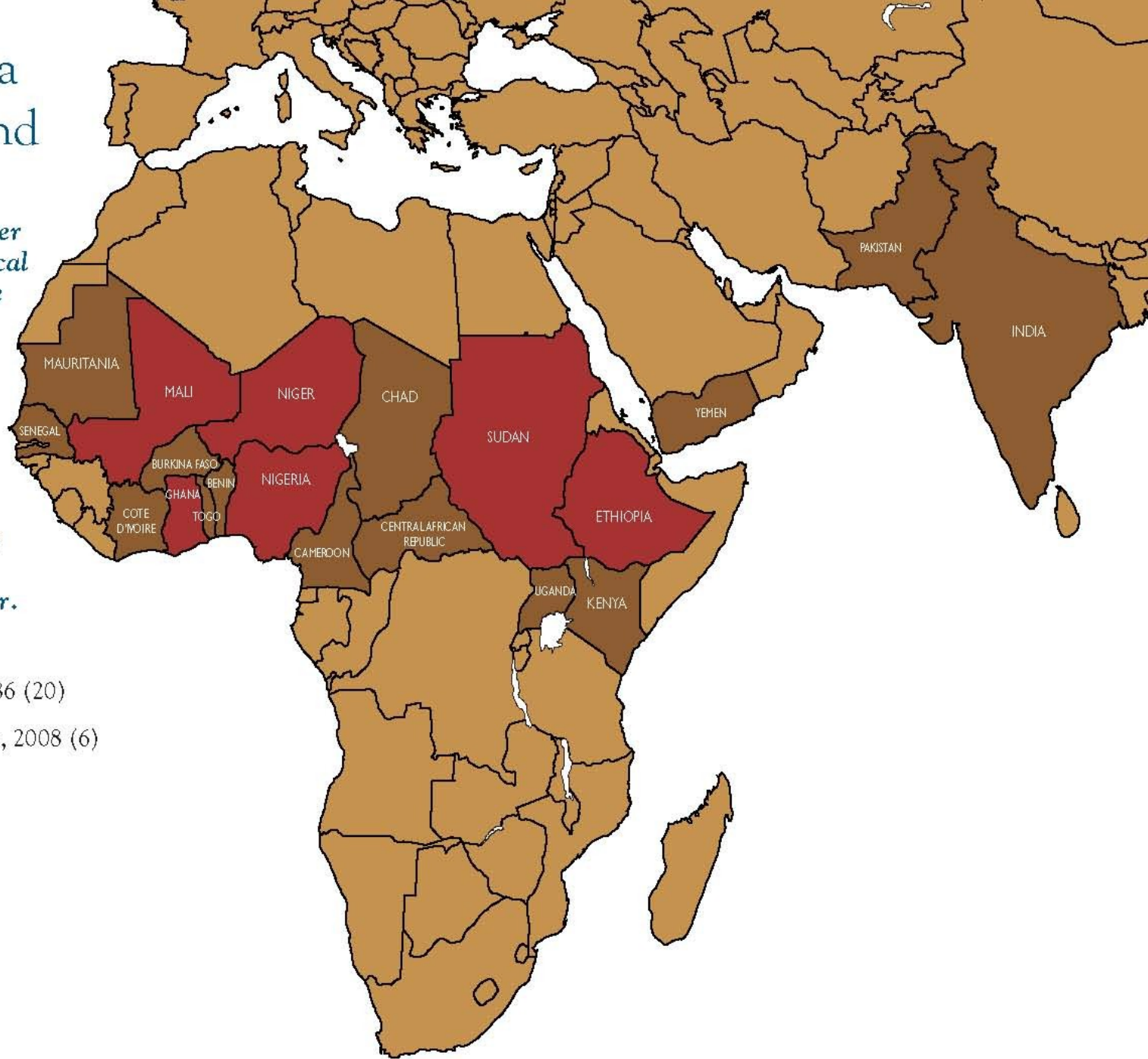


Humans become infected by drinking unfiltered water containing copepods (small crustaceans) which are infected with larvae of *D. medinensis* **1**. Following ingestion, the copepods die and release the larvae, which penetrate the host stomach and intestinal wall and enter the abdominal cavity and retroperitoneal space **2**. After maturation into adults and copulation, the male worms die and the females (length: 70 to 120 cm) migrate in the subcutaneous tissues towards the skin surface **3**. Approximately one year after infection, the female worm induces a blister on the skin, generally on the distal lower extremity, which ruptures. When this lesion comes into contact with water, a contact that the patient seeks to relieve the local discomfort, the female worm emerges and releases larvae **4**. The larvae are ingested by a copepod **5** and after two weeks (and two molts) have developed into infective larvae **6**. Ingestion of the copepods closes the cycle **1**.

Where Guinea Worm Is Found

When The Carter Center began to provide technical and financial assistance to national eradication programs in 1986, Guinea worm disease was found in 20 countries in Africa and Asia. Today the disease remains in six countries, all in Africa: Sudan, Ghana, Mali, Ethiopia, Nigeria, Niger.

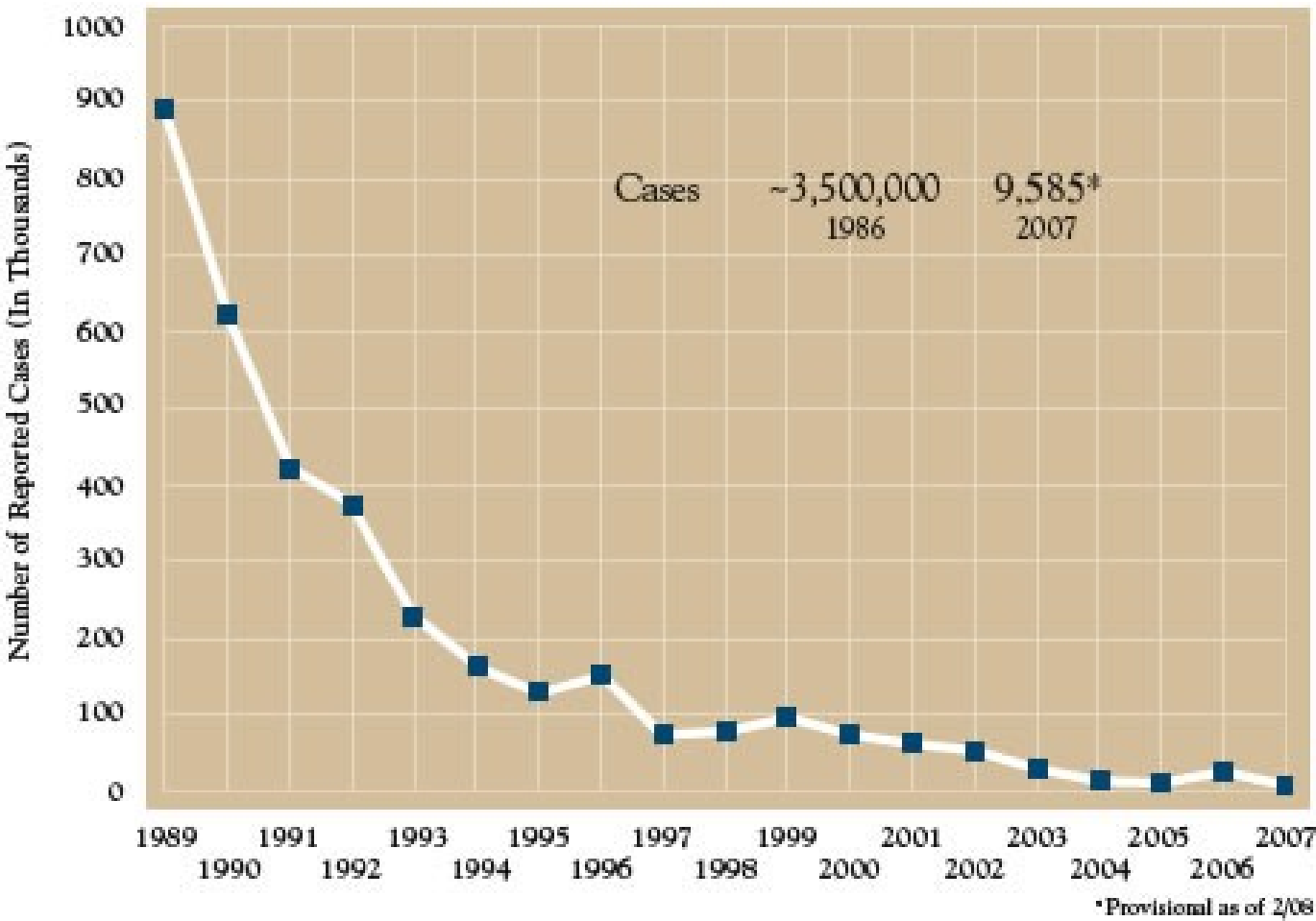
- Endemic countries, 1986 (20)
- Still endemic countries, 2008 (6)



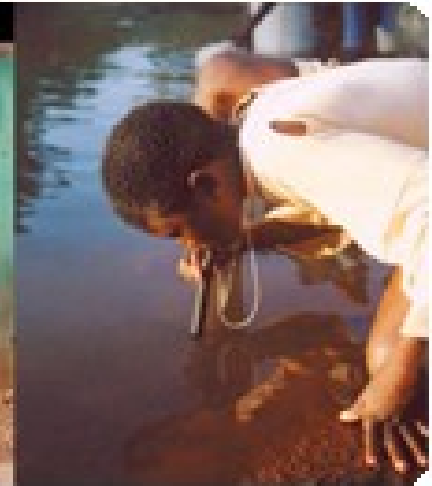


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Number of Reported Cases of Guinea Worm Disease by Year, 1989-2007



Treatment????



Dirofilaria immitis

Heartworm life cycle

